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ANNUAL PROGRESS REPORT (SUMMARY)

Report Prepared by Arthur W. Wase, Ph. D.

Date: 20 December, 1955

For Period 1 June to 20 December, 1955

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Contract: O N R:441:F H Q:mrl

Annual Rate: \$5000

Contractor: Hahnemann Medical College
Philadelphia, Pa.

Principal Investigator: Arthur W. Wase, Ph. D.
Assistant: Nancy Inforzato, B.S.

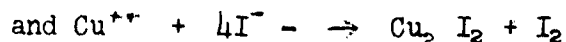
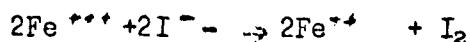
Title of Project: Enzymatic Regulation of Iodine Metabolism In the Thyroid

Objectives: To study the biochemical regulation of the production of
thyroid hormone.

Summary of Results:

1. A workable invitro system for the study of factors influencing the iodination of thyroglobulin has been established. The system employs buffered homogenates of whole thyroid tissue, I_{131} and appropriate accelerators.

2. Studies have been completed which indicate many cations to markedly influence the incorporation of I_{131} into the thyroglobulin moiety. Divalent cations behave differently than do the trivalent. Some of the results can be interpreted on the basis of known chemical reactions involving the oxidation of iodide ie.,



3. The Cu^{++} effect has been studied most extensively. Cu^{++} in concentration from 10^{-8} M to $.75 \times 10^{-4}$ M increases the incorporation of I_{131} from 100% over control (no added Cu^{++}) to 714 % over control. At 10^{-3} M the uptake drops to 397% of control value, at 10^{-2} M 135%.

4. The remarkable effect produced by Cu^{++} probably involves some selected SH groups, since the addition of SH reagents such as iodo acetate and p-chloromercuribenzoate shifts the Cu^{++} effect to the right (higher Cu^{++}

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for maximum incorporation), whereas glutathione shifts the reaction to the left.

5. The pH curve has been re-examined and confirmed. Two optima were noted, one at pH 4 and one at pH 7. The peak at pH 4 is low compared to that at pH 7, and it is believed to be due to the chemical oxidation of iodide to I_2 which occurs spontaneously at that low pH. Thermal activation of the system proceeds from 0°C to 37°C, thence inactivation occurred rapidly, probably due to denaturation of the active enzyme(s).

6. The role of the salivary glands and their influence on thyroid activity has been studied to permit accurate interpretation of findings. The salivary glands did not appreciably dehalogenate di-iodotyrosine, tri-iodo thyronine and thyroxine, but do appear to be functional via or in conjunction with the pituitary in regulating TSH production and utilization.

The energetics involving the iodination of thyroglobulin are currently under observation, ATPase levels of thyroid tissue in hyper, hypo and euthyroid states being studied. It is proposed to actively investigate the chemical nature of the Cu-enzyme, which we believe to exist, by isolation studies in the near future.